## REMARKS

Entry of the foregoing, reexamination and still further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. §1.116, are respectfully requested.

**Status**

As is correctly reflected on the cover sheet in the Official Action (but incorrectly stated on page 3 of the Action), claims 1, 6-13 and 18-38 were previously pending. Claims 18-30 were previously withdrawn from consideration; these claims are proposed to be cancelled by the foregoing amendment, in compliance with the restriction requirement. Claims 1, 6-13, and 18-38 stand finally rejected.

**Summary of Amendments**

By the foregoing amendments, claims 18-30 are proposed to be cancelled without prejudice or disclaimer to Applicants' filing of one or more divisional or other continuing applications directed to the cancelled subject matter.

Further by the foregoing amendments, claims 6, 9 and 31 are proposed to be worded as independent claims. Each of independent claims 1, 6, 9 and 31 is further proposed to be amended such that a cosmetically and/or dermatologically acceptable medium is recited as present in the claimed composition. As the compositions previously recited ingredients totaling at most 80% of the composition by weight, an appropriate medium is proposed to also be recited for the sake of clarity. This is supported by the specification, for example by page 5, lines 10-11. Moreover, each of independent claims 36 and 37 is proposed to be amended to recite that the claimed composition is topical and to further recite that there is present a cosmetically and/or dermatologically acceptable medium which separates

said at least one enzyme from said at least one precursor until the time of application. This, too, is amply supported by the original specification, for example, page 2, line 25 to page 3, line 4 and page 4, line 11 to page 5, line 14.

Applicants request that the foregoing amendments be entered to place the claims in better form for allowance, or as a minimum, to place them in better form for appeal.

**Rejection under 35 U.S.C. §103(a) – Boussouira et al. in view of Wheeler et al. and/or Berry et al.**

Claims 1, 6-13, and 31-38 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 6,153,205 to Boussouira et al. ("Boussouira et al.") in view of "*The biosynthetic pathway of vitamin C in higher plants*," by Glen L. Wheeler *et al.* ("Wheeler et al.") and/or U.S. Patent Application Publication No. 2002/0012979 A1 to Berry *et al.* ("Berry et al."). *See Official Action, Pages 3-6.* This rejection is respectfully traversed.

Before reaching the merits of the pending rejection, Applicants wish to stress that when applying 35 U.S.C. § 103, four tenets of patent law must be adhered to: (1) the claimed invention must be considered as a whole, (2) the references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination, (3) the references must be viewed without the benefit of impermissible hindsight vision, and (4) a reasonable expectation of success is the standard with which obviousness is determined. *See M.P.E.P. § 2141*, citing *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 (Fed. Cir. 1986). To establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference or to combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior

art reference(s) must teach or suggest all of the claim limitations. *See M.P.E.P. § 2142; see also SIBIA Neurosciences, Inc. v. Cadus Pharm. Corp.*, 225 F.3d 1349, 1356 (Fed. Cir. 2000) (explaining that if a reference needs to be modified to achieve the claimed invention "there must be a showing of a suggestion or motivation to modify the teachings of that reference to the claimed invention in order to support the obviousness conclusion.").

Applicants respectfully maintain that a *prima facie* case of obviousness has not been made out.

**Applicants' Claimed Invention**

In deciding whether a *prima facie* case of obviousness has been made out, it is important to keep in mind what Applicants have claimed. In the instant application, Applicants claim not simply ascorbic acid, but *compositions for topical application* comprising: (1) at least one ascorbic acid precursor that is *not* an ascorbic acid ester and that *is* L-galactono-1,4-lactone, L-gulono-1,4-lactone, D-glucorono-1,4-lactone, D-glucoronic acid, D-mannose, D-galacturonic acid, D-glucose, D-galactose, L-galactose, or mixtures thereof; (2) at least one enzyme that converts said ascorbic acid precursor to ascorbic acid; and (3) a cosmetically and/or dermatologically acceptable medium, with the enzyme and precursor each being present in a quantity of 0.1% to 10% by weight; see independent claim 1. Independent claim 6 further requires that the enzyme is selected from the group consisting of L-galactono-1,4-lactone dehydrogenase, L-galactose dehydrogenase, L-sorbosone dehydrogenase, L-gulono-1,4-lactone oxidase, and mixtures thereof. Independent claims 9 and 31 parallel claims 1 and 6, respectively, but require that the enzyme and precursor be packaged separately. Independent claims 36 and 37 also parallel claims 1 and 6,

respectively, but further require that the cosmetically and/or dermatologically acceptable medium separate the enzyme from the precursor until the time of application.

**Boussouira et al.**

The foundation for the pending § 103(a) rejection is based upon Boussouira et al. Boussouira et al., like Applicants, explain that while ascorbic acid, Vitamin C, has many beneficial attributes (*see, e.g., Boussouira et al. Column 1, Lines 19-24*), it is unstable and sensitive to external factors such as light and heat. *See Boussouira et al. Column 1, Lines 36-38.* Unfortunately, "[t]his instability goes against the desired efficacy and, what is more, can be the source of unpleasant sensations for the user, for example when the instability of the active agent leads to changes in the color and/or odor of the composition containing it." *Boussouira et al. Column 1, Lines 38-42.* Boussouira et al. then explain that several solutions have been proposed for stabilizing active ingredients such as Vitamin C, but those solutions have presented other difficulties, such as a decrease in efficacy and prevention of rapid release of Vitamin C in sufficient quantity. *See Boussouira et al. Column 1, Lines 49-59.* Boussouira et al. conclude that there is "a need for a topical application product containing vitamins used in cosmetics and/or dermatology, in which these vitamins conserve all their properties and thus their efficacy over time." *Boussouira et al. Column 1, Lines 60-63.*

According to Boussouira et al., EP 710,478 satisfy that need by using lipase with esters of Vitamin C. *See Boussouira et al. Column 1, Lines 64-67.* Boussouira et al. then announce that they have discovered another way to satisfy that need by introducing $C_6$ to $C_{22}$ alcohols into compositions having lipase and

Vitamin C esters. *See Boussouira et al. Column 2, Lines 1-4.* Boussouira et al.'s solution to the foregoing Vitamin C problem is to ensure that their products have: (1) a lipase; (2) at least one precursor of a vitamin wherein the precursor is an ester with a linear or branched, saturated or unsaturated chain containing 2 to 25 carbon atoms; (3) at least one $C_6$ to $C_{22}$ alcohol; and (4) a ratio of alcohol to precursor of 0.25 to 30/1. *See, e.g., Boussouira et al. Claim 1*; Abstract; Column 2, lines 8-13; Column 2, lines 66 to column 3, line 40.

It is respectfully submitted that the Examiner has mischaracterized the Boussouira et al. patent, and by doing so has made the reference appear to be more relevant than it actually is. The Boussouira et al. patent does not disclose a broad class of vitamin precursors and then specifically identify a particular type of precursor, the esters. The Examiner states on page 6 of the Action that Boussouira et al. do not teach that the esters are the only precursors that could be used. This statement is clearly in error, and it is upon this erroneous statement that the Examiner has built a house of cards, that is, it is the basis for obviousness rejection. Without this basis, the rejection must fall.

The fact is that the Boussouira et al. patent discloses esters, and indeed, only particular sorts of esters, as vitamin precursors. In the Summary of the Invention, Column 2, lines 7-18, Boussouira et al. state that their topical product comprises, as one essential, "at least one precursor of a vitamin used in cosmetics and/or dermatology which is an ester comprising at least one ester function with a linear or branched, saturated or unsaturated chain containing from 2 to 25 carbon atoms". Boussouira et al. further states, beginning in Column 2, line 66:

> As used herein, the term "precursor of a vitamin" refers to a esterified vitamin which is hydrolyzed on the skin to produce the free vitamin.

Thus, the patent's use of the term "precursor" is limited to esters. Boussouira et al. go on to describe further the characteristics of the esters in their composition. Nowhere is there a suggestion that their vitamin precursors can be anything other than esters.

Applicants emphasize that Boussouira et al. require that their vitamin precursors are esters and that those esters be hydrolyzed on the skin to produce the free vitamin. Boussouira et al. describe as another essential ingredient of their composition "at least one enzyme which is a lipase" (Column 2, lines 8-9). Boussouira et al. further provide a definition of a lipase in Column 2, lines 40-43:

> A lipase is an enzyme which is known to hydrolyze triglycerides into mono- and diglycerides, into glycerol and into free fatty acids.

**Boussouira et al. neither disclose nor suggest that their vitamin precursor can be other than an ester or that their enzyme can be other than lipase, which is an enzyme know to hydrolyze esters. Further, as noted above, they require that their ester be hydrolyzed on the skin.**

All of applicants' claims require an ascorbic acid precursor which is not an ester and which is L-galactono-1,4-lactone, L-gulono-1,4-lactone, D-glucorono-1,4-lactone, D-glucoronic acid, D-mannose, D-galacturonic acid, D-glucose, D-galactose, L-galactose, or a mixture thereof. Not one of these precursors is an ester. Boussouira et al. neither describe nor suggest any ascorbic acid precursors which are not esters, much less the particular precursors named in applicants' claims.

Applicants' claim 6 and its dependent claims and claim 37 and its dependent claims further specify that the enzyme is L-galactono-1,4-lactone dehydrogenase, L-galactose dehydrogenase, L-sorbosone dehydrogenase or L-gulono-1,4-lactone

oxidase or a mixture thereof. None of these is a lipase, as absolutely required by Boussouira et al.; none of these hydrolyze applicants' precursors, which is the reaction essential in Boussouira et al.'s invention.

**There is no motivation to modify and combine Boussouira et al. with Wheeler et al. or Berry et al. because Boussouira et al. teach away from Applicants' invention**

As explained above, to establish a *prima facie* case of obviousness, there must be some suggestion or motivation to modify the reference or to combine reference teachings. To arrive at Applicants' invention using Boussouira et al., one must modify **completely** Boussouira et al.'s requirement that the composition contain a vitamin *ester*. Applicants' compositions specifically ***exclude*** esters. There is nothing in Boussouira et al. to suggest to or motivate one of skill in the art to disregard that which Boussouira et al. have emphasized as critical to the success of their compositions. That is, there is nothing in Boussouira et al. that suggests or motivates one of skill to exclude the vitamin ester and insert in its stead a substance which cannot be hydrolyzed to the vitamin.

The Examiner has stated that "Boussouira clearly teaches compositions of ascorbic acid precursors, in combination with enzymes will effectively produce the active vitamin (col. 2 line 41 – col. 3 line 1)." *See Official Action, Page 6.* This statement misrepresents the very section of the reference which clearly teaches quite the opposite, i.e., that the reference's precursors must be esters which are hydrolyzed on the skin to release the vitamin. Applicants' precursors are not esters and are not hydrolyzed on the skin to release the vitamin. Not only do Boussouira et al. fail to suggest to or motivate one to modify its ester precursor attribute, it teaches away from doing so by emphasizing the beneficial combination of lipase, ester vitamin precursor, $C_6$ to $C_{22}$ alcohol, and alcohol to precursor ratio.

Moreover, ascorbic acid may be produced according to several pathways. Boussouira et al. rely upon the fact that ascorbic acid esters are naturally hydrolyzed by esterases, whereas Applicants' invention relies upon a synthesis mechanism involving sugars and oxidizing enzymes. Nothing in Boussouira et al. suggests to or motivates one to pursue a combination which makes use of a totally different pathway, especially in light of Boussouira et al.'s claim that only they and EP 710,478 (which shares the lipase plus ester combination) overcome past difficulties with active ingredients such as Vitamin C, and in light of Boussouira et al.'s requirement that their ester be hydrolyzed by lipase. Applicants' precursors are sugars, not esters, and their enzymes are specific dehydrogenases and oxidases which convert the sugars to ascorbic acid by oxidation, not by hydrolysis.

**Neither Wheeler et al. nor Berry et al. cure Boussouira et al.'s deficiencies**

Even if one of skill in the art were somehow prompted prior to Applicants' invention to disregard the ester precursor mandate, the lipase mandate and the hydrolysis mandate of Boussouira et al., Applicants maintain that the ordinary skilled person would not have looked to either Wheeler et al. or Berry et al. for guidance.

The Boussouira et al. patent is directed to topically-applicable compositions and methods for making such compositions containing a lipase, an ester vitamin precursor, a fatty alcohol, and a particular alcohol to precursor ratio. Wheeler et al. is directed not to compositions, let alone topically-applicable vitamin precursor ester/lipase/fatty alcohol compositions, but to a proposed pathway for ascorbate biosynthesis in higher plants. *See Wheeler et al., Page 368, ¶ 2.* As a result of the experiments conducted and the conclusions drawn therefrom, Wheeler et al. conclude only that "[w]e are now in a position to investigate the subcellular

localization and control of ***ascorbate*** biosynthesis in ***plants*** and, ultimately, to manipulate its content with ***potential benefits*** for human nutrition and plant resistance to oxidative stress." *Wheeler et al., Page 368, ¶ 4* (emphasis added). This is at most an invitation to experiment with ascorbate biosynthesis in plants to obtain some benefits for human nutrition. However, as the Examiner is well aware, such is not a proper basis for an obviousness rejection. And, of course, this invitation teaches nothing relevant to a totally different pathway to ascorbic acid and its use by Boussouira et al.

Applicants stress that the fact that Wheeler et al. happen to disclose that "ascorbic acid precursors 1-galactose and 1-galactono-1,4-lactone are converted to ascorbic acid by 1-galactose dehydrogenase" is of no moment. *See Official Action, Page 4.* Mere identification of each claimed element in the prior art is NOT sufficient to negate patentability. *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998). Instead, there "must be a teaching or suggestion within the prior art, or within the general knowledge of a person of ordinary skill in the filed of the invention, to look to particular sources of information, to select particular elements, and to combine them in the way they were combined by the inventor." *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 536 (Fed. Cir. 1998). Otherwise, sophisticated scientific fields would rarely, if ever, experience a patentable technical advance. *Rouffet*, 149 F.3d at 1357.

Similarly, the Berry et al. patent publication is as far afield from Boussouira et al. as is the Wheeler et al. reference. The Berry et al. publication relates not to compositions, let alone topically-applicable vitamin precursor ester/lipase/fatty alcohol compositions, but to methods for producing Vitamin C and esters thereof in microorganisms, genetically-modified microorganisms for producing Vitamin C and esters thereof, and to genetically modified plants for producing Vitamin C and esters

thereof. *See, e.g., Berry et al. Claims 1-72.* Berry et al. appear to have beneficially modified ascorbate biosynthesis in plants, which Wheeler et al. posited as a possible use of their theory of ascorbic acid biosynthesis. Applicants disagree that one of skill in the art would look to information on *genetically-modified microorganisms* for guidance herein.

Applicants respectfully reiterate that a *prima facie* case of obviousness has not been made out. Where is the crucial motivation or suggestion to combine the cited references? Indeed, it does not exist. There is simply no motivation or suggestion to combine and modify Boussouira et al., Wheeler et al., and/or Berry et al. as suggested by the Examiner.

With all due respect, it is submitted that is only hindsight interpretation of the references, coupled with an actual misunderstanding of what is taught by the primary Boussouira et al. reference, using applicants' own teachings as a guide through the maze of the prior art, which can lead to the present rejection. This is not a proper basis for a 35 U.S.C. §103 rejection.

In light of the foregoing, Applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) rejection of Claims 1, 6-13, and 31-38 over Boussouira et al. in view of Wheeler et al. and/or Berry et al.

## CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions relating to this response, or the application in general, it would be greatly appreciated if the Examiner would telephone the undersigned agent concerning such questions so that the prosecution of this application may be expedited.

Respectfully submitted,

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